DETAILED ACTION

1. Applicant's amendment filed 8/23/2010 is acknowledged and has been entered. Claims 1-38 cancelled. Claims 39-58 has been added. Claims 39-58 are pending. All of the arguments have been thoroughly reviewed and considered but are deemed moot in view of the Applicant's amendment cancelling the rejected claims 20-38. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejection

3. The claim rejections under 35 USC 112 first paragraph as lacking new matter is withdrawn in view of Applicant's amendment of Applicant's cancellation of the claims. The claim rejection under 35 USC 112 paragraph as being indefinite is withdrawn in view of Applicant's cancellation of the claims. The prior art rejections under 35 USC 103(a) are withdrawn in view of Applicant's cancellation of the claims.

New Ground(s) of Rejections

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 39 is indefinite in line 8 at "the at the surface of" because of redundant recitation. It is suggested deleting the repeated language recited above.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 39-52 are rejected under 35 USC 103(a) as being unpatentable over unpatentable Lockwood et al (Pharmaceutical Research, vol. 14, no. 11, 1997) in view of Lalchev et al (Biotechnology and Bioengineering, vol. XXIV, pages 2253-2262, 1982)

in view Wilde et al (citation made of record) and further in view of Ijiro et al (citation made of record).

Regarding claims 39-47 and 51-52, Lockward et al teach a method for concentration of a macromolecule in a liquid sample, the method comprising: providing a liquid medium, the liquid medium comprising the liquid sample and an interface layer, wherein the interface layer located on the surface of the liquid sample, fixes the macromolecule by chemical affinity (claim 42) and has a small volume as compared to liquid sample, forming a stabilized dispersion form by injection (claim 41) directly in the liquid sample of gaseous streams to form an interstitial medium constituting the foam; and resorbing the dispersion to reform the interface layer by drainage of the interstitial medium constituting the foam, wherein the macromolecule is enriched or concentrated in the interface layer which is collected as the foamate (see entire reference, such as e.g., abstract and sections entitled "The Foam Fractionation process" at pages 1511 and 11512 and "solution conditions and operational parameters at page 1513). Lockwood teaches wherein the macromolecule is protein, which inherently encompasses prions (abstract) and wherein the method allows for enrichment, purification and detection (claims 51 and 52) (see pages 1512 and 1513). Lockwood et al teaches that the method of foam fractionation can be used to separate DNA and protein (claim 43-44 and claims 46-47) (see bottom of page 1512, col. 2 bridging page 1513, col. 1). Lockwood cites Lalchev et al to support this assertion.

Lalchev et al teach the successful use of foam fractionation to separate DNA and protein (see e.g., abstract and pages 2254 and 2255).

Lockwood in view of Lalchev et al do not teach wherein the method comprises specific means of fixing the macromolecule, such as a molecule as required by the claim and do not teach wherein the dispersion is of the emulsion type rather than foam.

Wilde et al provides a general teaching of foam and emulsions for formation of interface layers and their stability during dispersion (see abstract and page 176). Wilde teaches that there are two classes of surface-active molecules. Wilde teaches that the first group of surface-active molecules is surfactants which include detergents, emulsifiers and lipids. Wilde teaches that they may be water or oil soluble, and usually form a compact adsorbed layer with a low interfacial tension. Wilde teaches that the second group of surface active molecules is polymers which include amphiphilic macromolecules, the most commonly used for proteins. Wilde teaches that they typically form a visco-elastic, irreversibly adsorbed layer (page 176). Wilde teaches throughout the review different surface properties for stabilization of foams and emulsion and further provides information on how different factors affect the stabilization and interfacial properties of the surface active molecules.

Ijiro et al. teach a method comprising forming a stabilized dispersion of an emulsion type from a medium comprising said liquid sample and an interface layer, wherein said interface is a gas-liquid interface, such as taught by Lockwood et al, said interface layer capable of fixing macromolecules (col. 2, lines 46-60; col. 3, line 35 to col. 4, line 61). Ijiro teaches wherein the fixing of the macromolecule is by chemical affinity ((col. 2, lines 46-60; col. 3, line 35 to col. 4, line 61). Ijiro et al teaches wherein the macromolecule is DNA (col. 3, lines 55-56). Likewise, Ijiro et al teaches wherein

the macromolecule is DNA and the molecule capable of fixing the DNA is functionalized with a probe to allow specific hybridization of the DNA or an intercalator (col. 3, line 54 to col. 4, line 13).

In view of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention that one of ordinary skill in the art could obtain predictable results of enriching DNA or protein using the known methods of foam/emulsion fractionation as taught by Lockwood et al in view of Lalchev et al and Ijiro et al. One of ordinary skill in the art at the time of the claimed invention would have been motivated to utilize foam/emulsion fractionation for the purpose of enriching nucleic acids or proteins or colloidal particles based on the advantages taught by Lockwood that foam fractionation has the potential to be a cost-effective component of purification/enrichment schemes (see abstract). It would have further been obvious to one of ordinary skill in the art at the time of the claimed invention to have been motivated to incorporate a molecule which fixes the macromolecule in the interface layer for the obvious benefit of detecting the amount of or concentrating nucleic acid polymers as suggested by Ijiro et al.

With regards to the claims 48-50, these claims merely recite a plethora of conventional nucleic acid manipulation reagents and methodologies, as well as well as routine optimization of reaction components, concentrations, and parameters as evidence by Lockwood et al and Ijiro et al. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability. Thus, one of ordinary skill in the art at the time of the claimed invention would have been motivated

to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations and/or expanded applications. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods using different means of mixing and fixing the DNA as claimed for the obvious benefit of detecting specific hybridization or for the benefit of controlling or detecting the orientation of the nucleic acid as taught by Ijiro et al (col. 7). The combination of Lockwood et al in view of Lalchev et al and Ijiro et al is *prima facie* obvious in the absence of secondary consideration.

Regarding claims 53-58, Lockwood et al in view of Wilder in view of Lalchev et al and further in view of Ijiro et al teach a method of enrichment/purification of a macromolecule, wherein the macromolecule is DNA or protein. Ijiro et al teach wherein the DNA is further used in hybridization reactions. The references do not teach wherein the DNA (macromolecule) is used in amplification reaction. However, it would have *prima facie* obvious to the ordinary artisan at the time of the claimed invention that the enriched or purified DNA or protein could be used in any of the plethora of well known biochemical reactions, such as nucleic acid amplification, sequencing, hybridization and etc. As noted earlier, these claims merely recite a plethora of conventional nucleic acid manipulation reagents and methodologies, as well as well as routine optimization or reaction components, concentrations, and parameters. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability. Thus, one of ordinary skill in the art would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations

an/or expanded applications. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods in the absence of secondary consideration.

Response to Arguments

8. Applicant traverses the rejections on the following grounds: Applicant summarizes the instant invention and states that Lockwood procedure does not teach an interface layer comprising at least one molecule able to fix a macromolecule or agglomerate of molecule or of particles initially contained in a liquid sample. Applicant states that since the reference fails to teach an interface layer, the reference necessarily fails to disclose resorbing the dispersion to reform the interface layer by drainage of the interstitial film constituting the foam or the emulsion, wherein the macromolecule is concentrated in the interface layer as claimed. Applicant states that Wilde fails to remedy the deficiencies of Lockwood et al. Applicant states that Lalchev et al does not involve the presence of an interfacial layer located at the surface. Applicant states and Lalchev et al do not teach the formation of dispersion followed by resorption allowing reconstitution of the interface located at the surface of the liquid sample. Applicant states that Ijiro et al does not teach or suggest forming a stabilized dispersion followed by a resorption step as claimed. Applicant concludes that the subject matter of the pending claims is not obvious over those references.

9. All of the arguments have been thoroughly reviewed and considered but are not found persuasive. In response to Applicant's arguments that the reference of Lockwood et al fails to provide an interface layer, the Examiner respectfully disagrees. Firstly, the

Federal Circuit discussed claim interpretation by the PTO in *In re Morris*, where the Federal Circuit noted "[A]s an initial matter, the PTO applies to the verbiage of the proposed claims the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's specification." *In re Morris*, 44 USPQ2d 1023, 1029 (Fed. Cir. 1997). The decision of the court in *In re Bigio*, 72 USPQ2d 1209 (Fed. Cir. 2004) strongly supports the breadth of interpretation. That court noted "[T]his court counsels the PTO to avoid the temptation to limit broad claim terms solely on the basis of specification passages." In concert with *Morris* and *Bigio* is the decision in *In re American Academy of Science Tech Center*, 70 USPQ2d 1827, 1834 (Fed. Cir. 2004), where the Federal Circuit noted "We have cautioned against reading limitations into a claim from the preferred embodiment described in the specification, even if it is the only embodiment described, absent clear disclaimer in the specification."

In this case, the specification at the bottom of page 6 bridging top of page 7 defines "interface layer" as a "monolayer (or virtually two-dimensional zone) located at the surface of the liquid sample (referred to as first liquid phase) comprising the macromolecule or the agglomerate to be concentrated. This layer, by virtue of its nature and specific properties, is able to provide the selective transfer of the macromolecule or of the agglomerate from the liquid sample to the interface layer and due to its tiny volume compared to the liquid sample, of concentrating aid macromolecule or said agglomerate". Lockwood et al meets the limitations of the claims as currently written.

Lockwood et al teach at page 1512, "there are two modes of operation by which foam fractionation may purify a protein, the difference lying in the relative-surface activities between the contaminates and the protein of interest". Lockwood teaches if the contaminants are more surface active, they will be removed via the foam, leaving he product in the residual solution. On the other hand, if the product of interest is more surface active, it will be enriched in the foam. Upon creation of a surface, the initial population of molecules at the interface is governed by a complex interaction of factors such as concentration, diffusivity, molecular flexibility and hydrophobicity. Lockwood teaches that due to high molecule weight, proteins are slow to absorb, typically exhibiting diffusion control. Lockwood states, "The affinity of a protein for the surface tends to be high as a result of the summed interaction of many hydrophobic force-driven points of attachment to the interface". Lockwood additionally depicts wherein the foamate is collected from the surface of the foam comprising the macromolecule of interest (Figure 1 and 2) by drainage of the interstitial film constituting the foam (pages 1511-13). Further, it is noted that Wilde provides additional examples of surface active molecules that fit in the class with foam, which includes emulsifiers and lipids. Thus, the formation of an interface layer as claimed by Applicant is within the ordinary artisan capabilities and would have been selected based on the practitioners desired results or merely routine optimization of known components (surface active molecules) capable of forming an interface layer.

With regards to Applicant's arguments concerning the lack of a teaching in Lockwood of a molecule which fixes the macromolecules, it is noted that the Examiner

cites a secondary reference9s) in order to provide this teaching and provides sufficient motivation for why an ordinary artisan would what to modify the teachings of Lockwood in order to incorporate a molecule which fixes a macromolecules (see Ijiro et al). Applicant is reminded that MPEP states that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

10. In response to Applicant's arguments concerning the teachings of Wilde, Lalchev et al and Ijiro et al, it is noted that the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, the rejections are not based on any one of the single references alone but rather is based on a combination of the teachings of Lockwood in view of Lalchev et al in view of Wilde et al and further in view of Ijiro et al. The Examiner maintains that the combination of the cited reference provides a *prima fa*cie case of obviousness.

Applicant's attention is directed to *KSR Int'l Co. v. Teleflex Inc.* (550 U.S.____, 127 S. Ct. 1727 (2007)) where the Supreme Court determined that "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If

this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103 (*KSR*, 550 U.S. at ____, 82 USPQ2d at 1397)." The Supreme Court also determined that "[t]he combination of familiar elements according to known methods is likely to be obvious when the combination does no more than yield predictable results (KSR, 550 U.S. at ___, 82 USPQ2d at 1395)." Applicant's arguments are not found persuasive to overcome the rejections noted above.

Conclusion

11. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637